

NEW SYNTHESSES OF  $\alpha$ -OXIMINO- $\alpha$ -HALOKETONES :  
REACTIONS OF  $\alpha$ -HALOKETONES WITH ALKYL THIONITRITES

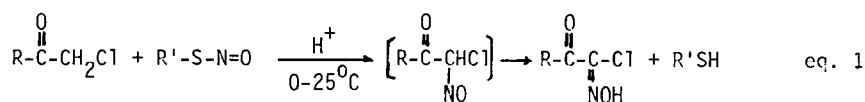
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Summary :  $\alpha$ -Oximino- $\alpha$ -haloketones were readily synthesized in good yields by treating  $\alpha$ -haloketones with alkyl thionitrites under mild conditions.

Since a quite stable tertiary butyl thionitrite<sup>1)</sup> was prepared by a simple reaction of tertiary butyl thiol with an equivalent amount of dinitrogen tetroxide, intensive studies on tertiary butyl thionitrite chemistry for organic syntheses such as unsymmetrical disulfides<sup>2)</sup>, N-(t-alkylthio)-p-benzoquinone imines<sup>3)</sup>, thioisulfones<sup>4)</sup>, and deaminations<sup>5)</sup> have been reported.

We now have found that various  $\alpha$ -haloketones reacted readily with alkyl thionitrites under mild conditions to afford the corresponding  $\alpha$ -oximino- $\alpha$ -haloketones in good yields as shown in eq. 1.



The  $\alpha$ -oximino- $\alpha$ -haloketones have been known to be biologically active compounds such as biocides and fungicides<sup>6)</sup> and also an intermediate for the synthesis of amino alcohols<sup>7)</sup>. Although nitrosyl chloride<sup>8)</sup> or alkyl nitrites<sup>9)</sup> were reported to be used for the syntheses of oximes, alkyl thionitrites appear to be better reagents for the nitrosation due both to the more facile cleavage of sulfur-nitrogen bond than that of oxygen-nitrogen bond of nitrites and also to the better leaving group of the thiolate moiety ( $\text{RS}^-$ ) than alkoxy group ( $\text{RO}^-$ ) in the nitrosation step. Indeed, tertiary butyl thionitrite reacted with chloromethyl ketone to give a better yield of the oxime than nitrites<sup>9a)</sup>.

A solution of tertiary butyl thionitrite<sup>1)</sup> (1.33 g, 11.1 mmole in anhydrous ether: 2 ml) was added onto a tertiarybutyl chloromethyl ketone solution (1.00 g, 7.4 mmole, anhydrous ether solution containing HCl gas: 15 ml) at 25°C for ca. 20 min. with stirring. The reaction mixture was then kept for 3 h with good stirring. The solution was concentrated and then solidified by addition of n-hexane (3.0 ml). The crude solid was recrystallized from carbon tetrachloride-chloroform (4:1) to give  $\alpha$ -oximino- $\alpha$ -chloro butyl ketone (1.03 g, 85%) which was identified by its <sup>1</sup>H nmr (ppm.  $\text{CDCl}_3$ ; 8.9, s, =NOH; 1.1, s, - $\text{CMe}_3$ ) and IR spectra, and elemental analysis (calc. C:44.05%, H:6.16%, N:8.56%, obs. C:44.26%, H:6.09%, N:8.65%). The results obtained are summarized in Table 1.

Table 1. Syntheses of  $\alpha$ -oximino- $\alpha$ -haloketones

Run	R	X	R'	$\frac{R'SNO}{RCOCH_2X}$	Reactn. Time(h)	Yield <sup>a)</sup> (%)	m.p.(°C)
1	Me	Cl	Me <sub>3</sub> C	2	3	82	102-3
2	Me	Cl	Me <sub>3</sub> C	1.5	3	82	
3	Me	Br	Me <sub>3</sub> C	2	3	43	103-4
4	Me	Cl	Me(CH <sub>2</sub> ) <sub>3</sub>	2	3-48 <sup>c</sup>	20 <sup>d</sup>	
5	Me(CH <sub>2</sub> ) <sub>3</sub>	Cl	Me <sub>3</sub> C	1.5	3	95 <sup>b</sup>	
6	Me <sub>3</sub> C	Cl	Me <sub>3</sub> C	1.5	3	85(95) <sup>b</sup>	131-2
7	Ph-OCH <sub>2</sub>	Cl	Me <sub>3</sub> C	1.5	3	95 <sup>b</sup>	166-7
8	Ph-CH <sub>2</sub>	Cl	Me <sub>3</sub> C	1.5	3	95 <sup>b</sup>	162-4
9	Ph	Cl	Me <sub>3</sub> C	1.5	3-48 <sup>c</sup>	20	132-3
10	Ph	Br	Me <sub>3</sub> C	1.5	3-48 <sup>c</sup>	10	

a) Isolated yield. b) Yield determined by <sup>1</sup>H nmr spectra. c) The yields were same after 3 h or 48 h reaction. d) Ca. 70% of starting material of  $\alpha$ -chloromethyl ketone and n-butyl disulfide were obtained after 48 h reaction along with the oxime.

In the case of  $\alpha$ -bromoketones (Runs 3 and 10), the yields of oximes were low. When n-butyl thionitrite was used as the nitrosation reagent instead of t-butyl thionitrite, the yield of oxime was also low (Run 4) due to its instability, where the thionitrite decomposed readily to the corresponding di-n-butyl disulfide<sup>10)</sup> during the reaction. The reaction appears to be initiated by forming nitroso compound intermediate, which converts quickly to the oxime by a proton migration.

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